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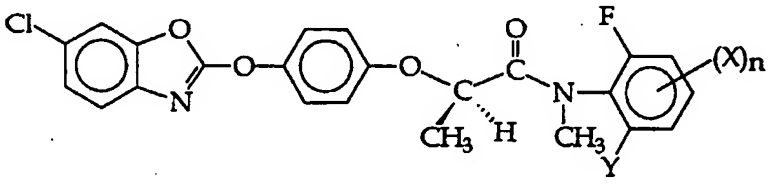
(54) Title: OPTICALLY ACTIVE HERBICIDAL (R)-PHENOXYPROPIONIC ACID-*N*-METHYL-*N*-2-FLUOROPHENYL AMIDES



(1)

(57) Abstract: The present invention relates to optically active herbicidal (R)-phenoxypropionic acid *N*-methyl-*N*-2-fluorophenyl amide compounds represented in the following formula (1), a method for preparing thereof, their use to prevent generation of barnyard grass produced from rice and composition as suitable herbicides, (I) wherein X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy,C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl; is hydrogen or fluoro; and n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

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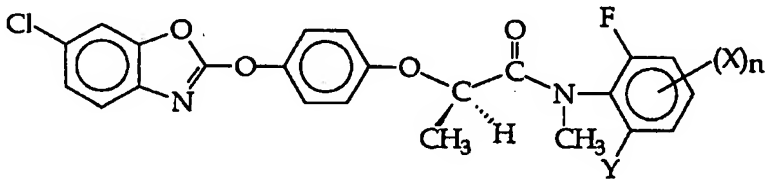
OPTICALLY ACTIVE HERBICIDAL (R)-PHENOXYPROPIONIC ACID-*N*-METHYL-*N*-2-FLUOROPHENYL AMIDES

【Technical Field】

The present invention relates to optically active herbicidal (R)-phenoxypropionic acid *N*-methyl-*N*-2-fluorophenyl amide compounds represented in the following formula (1), a method for preparing thereof, their use to prevent generation of barnyard grass produced from rice and composition as suitable herbicides,



(1)

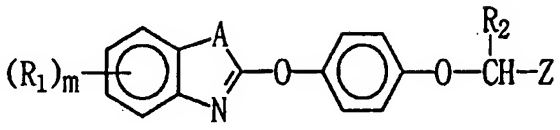
wherein X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl;

Y is hydrogen or fluoro; and

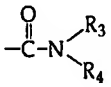
n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

【Background Art】

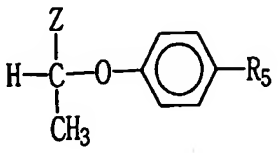
U.S. Pat. No. 4,130,413 discloses the compounds represented in the following formula (2),



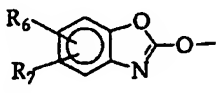
(2)

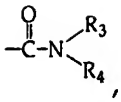
wherein $(R_1)_m$ is hydrogen, halogen, CF_3, NO_2, CN or alkyl; A is O, S or NH; R_2 is hydrogen or alkyl; Z is  , where R_3 and R_4 may be identical or different and represent hydrogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_3-C_6 cycloalkyl, C_1-C_4 alkoxy, or phenyl substituted with 1 to 3 substituents chosen from C_1-C_4 alkyl, C_1-C_6 alkoxy, halogen and CF_3.

U.S. Pat. No. 4,531,969 discloses the compounds represented in the following formula (3),

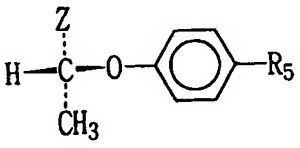


(3)

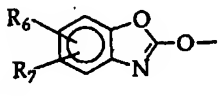
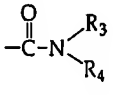
wherein R_5 is  , where R_6 is hydrogen or halogen; R_7 is

hydrogen or alkyl ; and Z is  , where R_3 and R_4 may be identical or different and represent hydrogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_3-C_6 cycloalkyl, C_1-C_4 alkoxy, or phenyl substituted with 1 to 3 substituents chosen from C_1-C_4 alkyl, C_1-C_6 alkoxy, halogen and CF_3.

U.S. Pat. No. 5,254,527 discloses the compounds represented in the following formula (4),



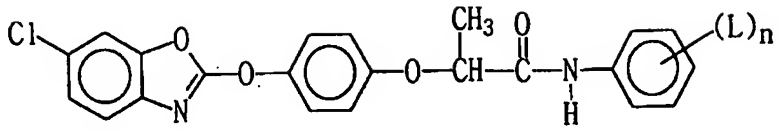
(4)

wherein R_5 is  , Z is  , where R_3 and R_4 may be identical or different and represent hydrogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, C_3-C_6 cycloalkyl, C_1-C_4 alkoxy, or phenyl substituted with 1 to 3 substituents chosen from C_1-C_4 alkyl, C_1-C_6 alkoxy, halogen and CF_3.

Even though some compounds of formula (1) of the present invention are disclosed in the above patents, none of the patents teach the synthesis of the compound of formula (1) and have tested the same for herbicidal activity.

JP Patent publication 2-11580 discloses the compound represented in the

following formula (5),

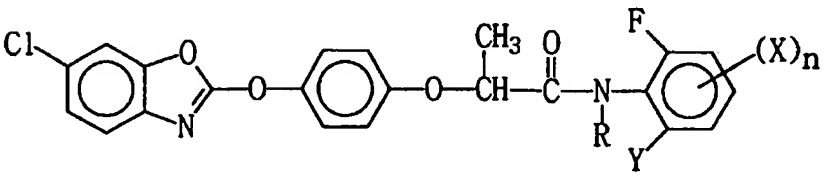


(5)

wherein L is low alkyl, halogen, methoxy, methoxyphenoxy, benzyloxy, methylthio or methylvinyl; and n is an integer of 0 to 2.

JP Patent publication sho 53-40767 and sho 54-112828 also disclose that phenoxypropionic acid amide derivatives have herbicidal activity.

Further, inventors of the present invention disclosed herbicidal phenoxypropionic acid *N*-alkyl-*N*-2-fluorophenyl amide compounds in International Pat. Publication No. WO 2000/05956.



(6)

Even though many of herbicides for rice have been recently developed and used, barnyard grass among weeds is the biggest problem in rice paddy.

Development of herbicides to control barnyard grass is an urgent to one who is in the field of agriculture. After transplanting young rice, herbicides, developed until now, cannot effectively control the production of barnyard grass so that it causes a huge damage to harvest. It has been reported that the

amount of rice harvest is decreased by 2% when barnyard grass is produced 1 week per 1 m^2, decreased by about 10% when produced 5 weeks per 1 m^2, decreased by about 19% when produced 10 weeks per 1 m^2 and decreased by about 35% when produced 20 weeks per 1 m^2.

Many different kinds of herbicides have been used for the purpose of controlling barnyard grass that damages in amount of harvest of rice. However, the herbicide with a broader herbicidal activity, environment-friendly property and cost-effectiveness is still in demand.

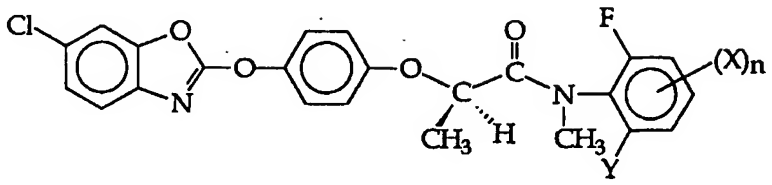
The inventors have intensively studied to provide herbicides to effectively control barnyard grass, and particularly, to find out selective herbicidal activity of phenoxypropionic acid *N*-alkyl-*N*-2-fluorophenyl amide compounds of formula (6). As a result, we completed this invention by finding that some phenoxypropionic acid *N*-alkyl-*N*-2-fluorophenyl amides of formula (6) exist as (R)- or (S)-stereoisomer, and (R)-stereoisomers provide higher stability to rice and better herbicidal activity compared to (S)-stereoisomers or mixtures thereof. This superior activity of (R)-stereoisomers is distinguished from the conventional inventions.

Therefore, an object of the present invention is to provide optically active herbicide compounds which exhibit excellent selectivity toward rice and prevent the production of harmful barnyard grass.

【Disclosure of Invention】

The present invention is to provide optically active herbicide phenoxypropionic acid *N*-methyl-*N*-2-fluorophenyl amides of formula (1) with

an excellent herbicidal activity as well as selective and remarkable stability toward rice,

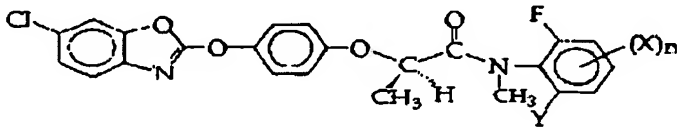


(1)

wherein X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl; Y is hydrogen or fluoro; and n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

The optically active compounds of formula (1) according to the present invention may be specified as the following Table 1.

Table 1



(1)

R	Y	X
CH_3	H	H
CH_2CH_3	H	H
CH_3	H	4-F
CH_3	H	3-F
CH_3	H	5-F
CH_3	H	4-Cl
CH_3	H	4-F, 5-F
CH_3	H	4-Br
CH_3	H	4- CH_3
CH_3	H	4-SCH_3
CH_3	H	4- CH_2CH_3
CH_3	H	4-propyl
CH_3	H	4-isopropyl
CH_3	H	4-butyl
CH_3	H	4-isobutyl

R	Y	X
CH_3	H	4-CO_2CH_3
CH_3	H	4-OCH_3
CH_3	H	4-OEt
CH_3	H	4-O-isopropyl
CH_3	H	4-O-allyl
CH_3	H	4-O-propyl
CH_3	F	H
CH_3	F	3-F
CH_3	F	4-F
CH_2CH_3	F	4-F
CH_3	F	4-Cl
CH_3	F	4-Br
CH_3	F	4-CH_3
CH_3	F	4- CH_2CH_3
CH_3	F	4-propyl
CH_3	F	4-isopropyl
CH_3	F	4-cyclopropyl
CH_3	F	4-butyl
CH_3	F	4-isobutyl

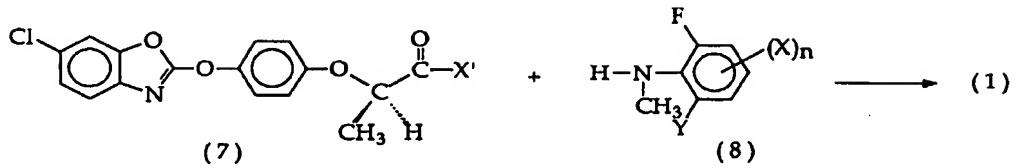
R	Y	X
CH_3	F	4-OCH_3
CH_3	F	4-OEt
CH_3	F	4-O-isopropyl
CH_3	F	4-O-propyl
CH_3	F	3-F, 5-F
CH_3	H	5-F
CH_3	H	5-Cl
CH_3	H	5-Br
CH_3	H	5-CH_3
CH_3	H	5-SCH_3
CH_3	H	5-CH_2CH_3
CH_3	H	5-propyl
CH_3	H	5-isopropyl
CH_3	H	5-cyclopropyl
CH_3	H	5- butyl
CH_3	H	5-isobutyl
CH_3	H	5-OCH_3
CH_3	H	4-OEt

R	Y	X
CH_3	H	5-O-isopropyl
CH_3	H	5-O-propyl
CH_3	H	5-O-allyl
CH_3	F	5-H
CH_3	F	5-F
CH_3	F	5-Cl
CH_3	F	5-Br
CH_3	F	5-CH_3
CH_3	F	5-CH_2CH_3
CH_3	F	5-propyl
CH_3	F	5-isopropyl
CH_3	F	5-cyclopropyl
CH_3	F	5-n-butyl
CH_3	F	5-isobutyl
CH_3	F	5-OCH_3
CH_3	F	5-OEt
CH_3	F	5-O-isopropyl
CH_3	F	5-O-propyl

The optically active compounds of formula (1) according to this invention may be synthesized by employing a conventional method represented in the following Scheme 1, reacting a compound of formula (7)

with a compound of formula (8),

Scheme 1

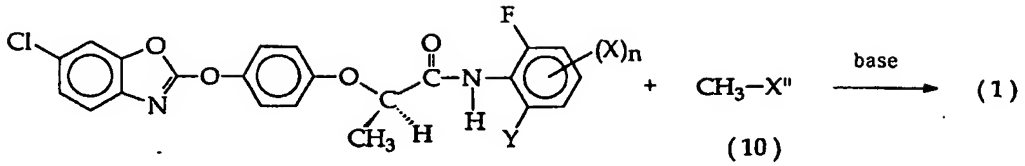


wherein X' is OH, Cl, Br, or phenoxy; X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl; Y is hydrogen or fluoro; and n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

In the method according to Scheme 1, it is performed preferably to use a binder such as triphenylphosphine and an organic base such as triethylamine or pyridine at a temperature of 0 to 100℃ in an inert solvent such as ethers like tetrahydrofuran, ethyethyl acetate, acetonitrile, toluene, xylene, hexane, methylene chloride, carbon tetrachloride, dichloroethane or the like. After the solvent is evaporated, the crude product is purified by column chromatography.

Another method for preparing the compounds (1) represented in the following Scheme 2 is an alkylation of a compound of formula (9) to a compound of formula (10),

Scheme 2

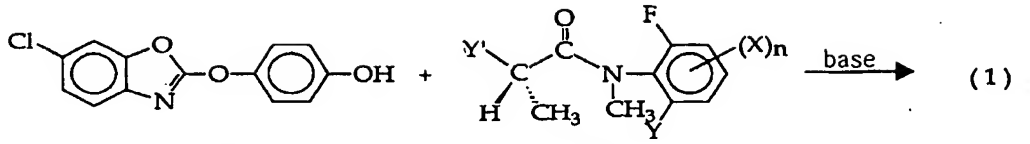


wherein X" is Cl, Br, I, benzenesulfonyloxy, toluenesulfonyloxy, methanesulfonyloxy or low alkyl sulfate; and X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl; Y is hydrogen or fluoro; and n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

In scheme 2, it is performed preferably using a strong base which is enough to pull out a hydrogen from amide, NH. Examples of a strong base include NaOH, KOH, LiOH, NaH, n-BuLi, LDA, and the like. The reaction is performed at a temperature of -78 to 50℃ in an inert solvent such as ethers like ethylether, dioxane or tetrahydrofuran or hydrocarbons like hexane.

Another method for preparing the compounds (1) represented in the following Scheme 3 is a reaction of a compound of formula (11) with a compound of formula (12) in the presence of a base,

Scheme 3



(11) (12)

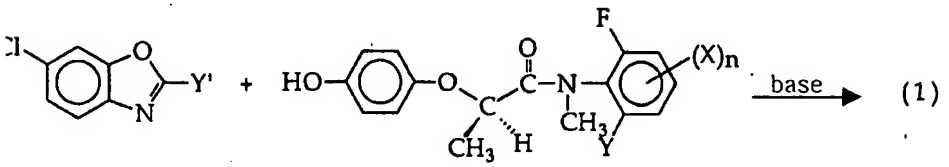
wherein Y' is halogen, alkylsulfonyloxy, haloalkylsulfonyloxy, benzenesulfonyloxy or toluenesulfonyloxy; X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl; Y is hydrogen or fluoro; and n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

In Scheme 3, examples of the base include inorganic bases of alkali metal hydroxides such as sodium hydroxide and potassium hydroxide, alkali metal carbonates such as sodium carbonate and potassium carbonate, alkali metal hydrogen carbonates such as sodium hydrogencarbonate and potassium hydrogencarbonate; and organic bases such as triethylamine, *N,N*-dimethylaniline, pyridine and 1,8-diazabicyclo[5,4,0]undec-7-ene.

A phase transition catalyst such as tetra-*n*-butylammonium bromide or 18-crown-6-[1,4,7,10,13,16-hexaoctacyclooctadecane] may be added to rapidly complete the reaction, if necessary. Further, one or more than two solvents may be used, if deemed necessary. Examples of the inert organic solvent include ketones such as acetone; aromatic hydrocarbons such as toluene, xylene and

chlorobenzene; aliphatic hydrocarbons such as petroleum ether and ligroin; ethers such as diethylether, tetrahydrofuran and dioxane; nitrites such as acetonitrile and propionitrile; and amides such as *N,N*-dimethylformamide, *N,N*-dimethylacetamide, and *N*-methylpyrrolidone. A reaction is carried out at a temperature of from 0℃ to reflux, preferably at 5 to 50℃, for 1 to 24 hour(s) to afford the desired product with high yield.

Another method for preparing the optically active compound (1) represented in the following Scheme 4 is a reaction of a compound of formula (13) with a compound of formula (14) in the presence of a base,



(13) (14)

wherein Y' is halogen, alkylsulfonyloxy, haloalkylsulfonyloxy, benzenesulfonyloxy or toluenesulfonyloxy; X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl; Y is hydrogen or fluoro; and n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

In Scheme 4, examples of the base include inorganic bases of alkali

metal hydroxides such as sodium hydroxide and potassium hydroxide, alkali metal carbonates such as sodium carbonate and potassium carbonate, alkali metal hydrogencarbonates such as sodium hydrogencarbonate and potassium hydrogencarbonate; and organic bases such as triethylamine, *N,N*-dimethylaniline, pyridine, picoline, quinoline, and 1,8-diazabicyclo[5,4,0]undec-7-ene.

A phase transition catalyst such as tetra-*n*-butylammonium bromide or 18-crown-6[1,4,7,10,13,16-hexaoctacyclooctadecane] may be used, if necessary. Further, more than one solvent may be used if deemed necessary. Examples of the inert organic solvent include ketones such as acetone and butanone; aromatic hydrocarbons such as benzene, toluene, xylene and chlorobenzene; aliphatic hydrocarbons such as petroleum ether, and ligroin; ethers such as diethylether, tetrahydrofuran and dioxane; nitriles such as acetonitrile or propionitrile; and amides such as *N,N*-dimethylformamide, *N,N*-dimethyl acetamide and *N*-methylpyrrolidone. A reaction is carried at a temperature of from 0℃ to reflux, preferably at 20 to 100℃ for 1 to 24 hour(s) to afford the desired product with high yield.

The present invention will be further illustrated by the following examples. However, they should not be construed as limiting the scope of this invention defined by the appended claims.

【Examples】

Example 1: Preparation of (S)-2-bromo-propionic acid-*N*-(2-fluorophenyl)-*N*-methyl amide

(S)-2-Bromopropionic acid(3.4 g, 0.022 mol) and 2-fluoroaniline(3 g, 0.024 mol) were dissolved in 50 ml of chloroform and cooled to 0℃. Dicyclohexylcarbodiimide(5 g, 0.024 mol) dissolved in 10 ml of chloroform was slowly injected through a syringe. The temperature of the reaction mixture was raised to room temperature and the reaction mixture was stirred for 1 hour. Solid remained during the reaction was filtered out and washed twice with 20 ml of chloroform. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography (eluent; ethyl acetate/*n*-hexane=1/3) to afford 5 g of the target product.

^{1}H-NMR($CDCl_3$) : δ1.7(3H, d), 3.24(3H, s), 4.16(0.7H, q), 4.34(0.3H, q), 7.13-7.48(4H, m)

Example 2: Preparation of (R)-2-(4-hydroxyphenoxy)propionic acid-*N*-(2-fluorophenyl)-*N*-methyl amide

(S)-2-bromo-propionic acid-*N*-(2-fluorophenyl)-*N*-methyl amide (18.2 g, 0.07 mol), hydroquinone (7 g, 0.064 mol), potassium carbonate (10.54 g, 0.076 mol) and tetra-*n*-butylammonium bromide (1 g) were dissolved in 350 ml of acetonitrile and heated at reflux for 6 hours. The reaction mixture was cooled to room temperature and solid remained during the reaction was filtered out. The filtrate was concentrated under reduced pressure and the crude product was

purified by column chromatography(eluent: ethyl acetate/*n*-hexane=1/2) to afford 16 g of the target product.

^{1}H-NMR($CDCl_3$) : δ1.42(3H, t), 3.25(3H, s), 4.56(1H, q), 6.5-7.4(8H, m)

Example 3: Preparation of (R)-2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]propionic acid-*N*-(2-fluorophenyl)-*N*-methyl amide

(R)-2-(4-hydroxyphenoxy)propionic acid-*N*-(2-fluorophenyl)-*N*-methyl amide (11.5 g, 0.04 mol), 2,6-dichlorobenzoxazole (6.85 g, 0.036 mol), potassium carbonate (6 g, 0.043 mol) and tetra-*n*-butylammonium bromide (1 g) were dissolved in 300 ml of acetonitrile and heated at reflux for 7 hours. The reaction mixture was cooled to room temperature and solid remained during the reaction was filtered out. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography (eluent: ethyl acetate/*n*-hexane=1/3) to afford 12.5 g of the target product.

^{1}H-NMR($CDCl_3$) : δ1.42(3H, t), 3.3(3H, s), 4.62(1H, m), 6.8-7.4(11H, m)

Example 4: Preparation of (R)-2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]propionic acid-*N*-(2-fluorophenyl)-*N*-methyl amide

(R)-2-[4-(6-chloro-2-benzoxazoyloxy)-phenoxy]propionic acid (346.7 mg, 1 mmol) was dissolved in 10 ml of tetrahydrofuran. 2-Fluoroaniline(111.12 mg, 1 mmol), triphenylphosphine(393.4 mg, 1.5 mmol), triethylamine(0.15 ml, 1 mmol) and carbon tetrachloride(1 ml) were added sequentially and heated at

reflux for 8 hours. The reaction mixture was cooled to room temperature and acidified with 5% hydrochloric acid, followed by addition of water. The acidified reaction mixture was extracted three times with ethyl acetate. The combined organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography(eluent: ethyl acetate/*n*-hexane=1/4) to afford 200 mg of the target product.

m.p : 132-136℃

^{1}H-NMR($CDCl_3$) : δ1.7(3H, d), 4.81(1H, q), 7.05-7.45(10H, m), 8.35(1H, m), 8.5(1H, br)

Example 5: Preparation of (R)-2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]propionic acid-*N*-(2-fluorophenyl)-*N*-methyl Amide

(R)-2-[4-(6-chloro-2-benzoxazoyloxy)-phenoxy]propionic acid-*N*-(2-fluorophenyl)amide (100 mg, 0.24 mmol) was dissolved in 10 ml of anhydrous tetrahydrofuran and 60% NaH(10 mg, 0.24 mmol) and CH_3I(34 mg, 0.24 mmol) were added sequentially at 0℃. The reaction mixture was stirred at room temperature for 5 hours. Ice water was poured to the reaction mixture and it was extracted three times with ethyl acetate. The combined organic solvent layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography(eluent: ethyl acetate/*n*-hexane=1/2) to afford 75 mg of the target product.

^{1}H-NMR($CDCl_3$) : δ1.42(3H, t), 3.3(3H, s), 4.62(1H, m), 6.8-7.4(11H, m)

Example 6: Preparation of (R)-2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]propionic acid-*N*-(2-fluorophenyl)-*N*-methyl amide

(R)-2-[4-(6-chloro-2-benzoxazoyloxy)-phenoxy]propionic acid(346.7 mg, 1 mmol) was dissolved in 10 ml of tetrahydrofuran and *N*-methyl-2-fluoroaniline(125 mg, 1 mmol), triphenylphosphine(393.4 mg, 1.5 mmol), triethylamine(0.15 ml, 1 mmol) and carbon tetrachloride(1 ml) were added sequentially and the reaction was heated at reflux for 12 hours. The reaction mixture was cooled to room temperature and acidified with 5% hydrochloric acid, followed by addition of water. The acidified reaction mixture was extracted three times with ethyl acetate. The combined organic solvent layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography(eluent: ethyl acetate/*n*-hexane=1/2) to afford 100 mg of the target product.

Example 7: Preparation of (R)-2-[4-(6-chloro-2-benzoxazolyloxy-phenoxy)propionic acid-*N*-methyl-*N*-(2,4,5-trifluorophenyl)amide

(R)-2-[4-(6-chloro-2-benzoxazoyloxy)-phenoxy]propionic acid (0.693 g, 2 mmol) was dissolved in 15 ml of tetrahydrofuran and *N*-methyl-2,4,5-trifluoroaniline(0.322 g, 2 mmol), triphenylphosphine(0.78g, 2 mmol), triethylamine(0.4 ml) and carbon tetrachloride(2 ml) were added sequentially and then the reaction mixture was heated at reflux for 18 hours. The reaction

mixture was cooled to room temperature and acidified with 5% hydrochloric acid. The acidified reaction mixture was extracted three times with ethyl acetate. The combined organic solvent layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography(eluent: ethyl acetate/*n*-hexane=1/2) to afford 250 mg of the target product.

^{1}H-NMR($CDCl_3$) : δ1.42(3H, d), 3.2(3H, s), 4.65(1H, m), 6.6-7.4(9H, m)

Example 8: Preparation of (R)-2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]propionic acid-*N*-methyl-*N*-(2,6-difluoro-phenyl)amide

(R)-2-[4-(6-chloro-2-benzoxazoyloxy)-phenoxy]propionic acid(0.693 g, 2 mmol) and *N*-methyl-2,6-difluoroaniline(0.284 g, 2 mmol) were dissolved in 20 ml of tetrahydrofuran and triphenylphosphine(0.78 g, 2 mmol), triethylamine(0.42 ml) and carbon tetrachloride(2 ml) were added sequentially. The reaction mixture was heated at reflux for 16 hours. The reaction mixture was cooled to room temperature and acidified with 5% hydrochloric acid. The acidified reaction mixture was extracted three times with ethyl acetate. The combined organic solvent layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography(eluent: ethyl acetate/*n*-hexane=1/2) to afford 205 mg of the target product.

^{1}H-NMR($CDCl_3$) : δ1.4(3H, d), 3.3(3H, s), 4.62(1H, q), 6.8−7.4(10H, m)

Example 9: Preparation of (R)-2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]propionic acid-*N*-(2,4-difluorophenyl)-*N*-methyl amide

(R)-2-[4-(6-chloro-2-benzoxazoyloxy)-phenoxy]propionic acid(0.693 g, 2 mmol) was dissolved in 15 ml of tetrahydrofuran and *N*-methyl-2,4-difluoroaniline(0.284 g, 2 mmol), triphenylphosphine(0.78 g, 2 mmol), triethylamine(0.42 ml) and carbon tetrachloride(2 ml) were added sequentially. The reaction mixture was heated at reflux for 12 hours. The reaction mixture was cooled to room temperature and acidified with 5% hydrochloric acid, followed by addition of water. The acidified reaction mixture was extracted three times with ethyl acetate. The combined organic solvent layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography(eluent: ethyl acetate/*n*-hexane=1/2) to afford 230 mg of the target product.

^{1}H-NMR($CDCl_3$) : δ1.4(3H, d), 3.2(3H, s), 4.6(1H, q), 6.6-7.2(10H, m)

Example 10: Preparation of (R)-2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]propionic acid-*N*-methyl-*N*-(2,3,6-trifluorophenyl)amide

(R)-2-[4-(6-chloro-2-benzoxazoyloxy)-phenoxy]propionic acid(0.693g, 2 mmol) was added to 6 ml of thionyl chloride and the reaction mixture was heated at reflux for 2 hours. Excess of thionyl chloride was removed under reduced pressure and 3 ml of anhydrous tetrahydrofuran was added to it. A solution of *N*-methyl-2,3,6-trifluoroaniline(0.32 g, 2 mmol) and triethyl amine(0.42 ml) in anhydrous tetrahydrofuran(10 ml) was added slowly to the

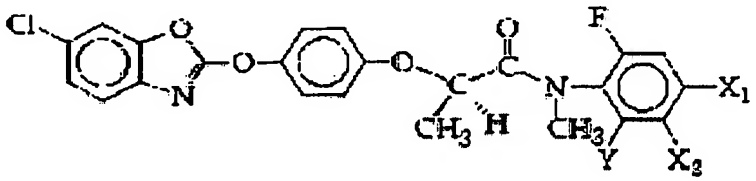
reaction mixture at 0℃. The mixture was stirred at 0℃ for 30 minutes and stirred at room temperature for additional 1 hour. After pouring water the reaction mixture was extracted three times with ethyl acetate. The combined organic solvent layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography(eluent: ethyl acetate/*n*-hexane=1/2) to afford 240 mg of the target product.

^{1}H-NMR($CDCl_3$) : δ1.45(3H, d), 3.25(3H, s), 4.6(1H, q), 6.7-7.4(9H, m)

Examples 11-16

The compounds represented in the following Table 2 were prepared by the same procedure of example 10 except using of aniline compounds instead of *N*-methyl-2,3,6-trifluoroaniline.

Table 2



Classification	X_1	X_2	^{1}H-NMR($CDCl_3$)
Example 11	H	CH_3	1.42(3H, t), 2.3(3H, s), 3.25(3H, s), 4.62 (1H, m), 6.8-7.4(10H, m)
Example 12	Cl	H	1.42(3H, t), 3.3(3H, s), 4.62(1H, m), 6.7-7.5(10H, m)
Example 13	H	F	1.42(3H, t), 3.3(3H, s), 4.62(1H, m), 6.5-7.4(10H, m)
Example 14	CH_3	H	1.42(3H, t), 2.38(3H, s), 3.25(3H, s), 4.62(1H, m), 6.8-7.4(10H, m)
Example 15	OCH_3	H	1.42(3H,t), 3.25(3H, s), 3.8(3H, s), 4.65(1H, m), 6.65-7.45(10H, m)
Example 16	OCH_2CH_3	H	1.25(3H, t), 1.42(3H, t), 3.25(3H, s), 4.0(2H, q), 4.62(1H, m), 6.65-7.42(10H. m)

Formulation

In order to use the compounds according to the present invention as herbicides, they should be formulated in such a suitable type such as wettable powder, emulsions, granules, dusts, suspensions and solutions by combining a carrier, a surfactant, a dispersing agent or a supplement agent. Many of these may be applied directly or after diluted with suitable media. Formulations can be prepared at spray volume of from hundreds liters to thousands liters per hectare. The formulations contain about 0.1% to 99% by weight of active ingredient(s) and 0.1% to 20% surfactant(s) or 0% to 99.9% solid or liquid diluent(s) are recommended to be added. The formulations will contain these

ingredients in the following approximate proportions shown in Table 3.

Table 3

Formulations	Wt. %		
	Active ingredient	Diluent	Surfactant
Wettable powder	10-90	0-74	1-10
Suspension	3-50	40-95	0-15
Emulsion, solution	3-50	40-95	0-15
Granule	0.1-95	5-99.9	1-15

The proportion of active ingredients depends on the intended use. Higher ratio of a surfactant is sometimes desired to active ingredients and is achieved by incorporation into the formulation or tank mixing.

Solid diluents with high absorption are preferred for wettable powder. Liquid diluents and solvents are preferred to be stable against phase separation at 0℃. All the formulations may contain a small amount of additives to prevent forming, caking, corrosion and growth of microorganisms.

According to conventional methods to prepare the composition, solutions can be made only by blending ingredients and fine solids by blending and pulverizing with hammer-mill. Suspensions can be made by wet-milling and granules can be made by spraying the active ingredients on performed granular carrier.

Preparation examples of typical formulations are as follows.

Formulation 1: Wettable Powder

The ingredients are thoroughly blended, re-blended after spraying liquid surfactant on the solid ingredients and hammer-milled until all the solids are essentially under 100 μm.

Active ingredient (Compound of Example 3)	20 wt.%
Dodecylphenol polyethylene glycol ether	2 wt.%
Sodium ligninsulfonate	4 wt.%
Sodium silicon aluminate	6 wt.%
Montmorillonite	68 wt.%

Formulation 2: Wettable Powder

The ingredients are blended, hammer-milled until all the solids are under 25 μm and packaged.

Active ingredient (Compound of Example 3)	80 wt.%
Sodium alkyl naphthalenesulfonate	2 wt.%
Sodium ligninsulfonate	2 wt.%
Synthetic amorphous silica	3 wt.%
Kaolinite	13 wt.%

Formulation 3: Emulsion

The ingredients are mixed and homogeneously dissolved to give emulsions.

Active ingredient (Compound of Example 3)	30 wt.%
Cyclohexanone	20 wt.%

Polyoxyethylene alkylaryl ether	11 wt.%
Calcium alkylbenzenesulfonate	4 wt.%
Methylnaphthalene	35 wt.%

Formulation 4: Granule

The ingredients were thoroughly blended. 20 parts by weight of water was added to 100 parts of weight the ingredient mixture. The ingredient mixture was granulated with a size of 14 to 32 mesh by using extrusive granulator and dried.

Active ingredient (Compound of Example 3)	5 wt.%
Sodium laurylalcoholsulfonate	2 wt.%
Sodium ligninsulfonate	5 wt.%
Carboxymethyl cellulose	2 wt. %
Potassium sulfate	16 wt.%
Plaster	70 wt.%

The formulations according to this invention were sprayed with diluting to a certain concentration.

Utility

The compounds according to the present invention represent high activity as leaf treatment herbicides for rice and especially effective in rice due to an excellent control of barnyard grass.

The active ingredients can be used from 10 g to 4 kg per hectare, preferably from 50 g to 400 g. The amount of the compounds of the present invention depends on the amount and size of weeds and formulations. The herbicides of the present invention can be used as alone or in combination with other herbicides, insecticides or bactericides. Especially it is essential to add one agent selected from the group consisting of bentazon, quinclorac, propanil, simetryn, 2,4-D, fenoxaprop-ethyl, linuron, MCPA, azafenidin, carfentrazone, molinate, thiobencarb, pendimethalin, bensulfuron-methyl, pyrazosulfuron-ethyl, metsulfuron-methyl, thifensulfuron-methyl, tribenuron-methyl, trifluralin, amidosulfuron, bromoxynil, butachlor, mecoprop, metribuzin, bifenox, benfuresate, isoproturon, cyhalofop-butyl, mefenaset, fentrazamide, pyriminobac-methyl, bispyribac sodium, azimsulfruon, cyclosulfamuron, pyanchor, and mixtures thereof.

The herbicidal effect of the compounds of this invention was tested and the examples are as follows.

Experimental Example 1: Leaf Treatment Test

Seeds of rice, wheat, barley, corn, cotton, barnyard grass, common sorgum, large crabgrass and fall panicum were seeded at a pot with a surface area of 600 cm^2. When barnyard grass grown in a green house kept at 20 - 30 ℃ had three leaves, wettable powder prepared by mixing 1 part by weight of the active compound, 5 parts by weight of acetone and 1 part by weight of emulsifier and diluted with water was applied directly to the leaves in 2000 L per hectare. The concentration of the spray liquid was so chosen the particular

amounts of the active compound desired. 14 days after the treatment, the degree of damage to the plants was rated in % damage in comparison to the development of untreated control.

0%	no effect (same as untreated control)
20%	slight effect
70%	herbicidal effect
100%	total destruction

In the test, the active compound(s) of formula (1) according to the invention exhibited an excellent selectivity toward the plants and herbicidal activity against weeds.

Table 4

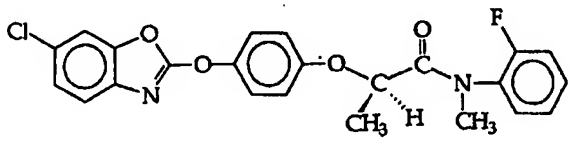
Abbr.	Scientific Name	English Name
ORYSA	Oryza sativa L. cv. Dongjin	Rice
ECHCG	Echinochloa crus-galli Beauv. var. caudata Kitagawa	Barnyard grass

Among the compounds of formula (1), herbicidal activity of (R)-2-[4-chloro-2-benzoxazoyloxy]-phenoxy]propionic acid-*N*-(2-flurorophenyl)-*N*-methyl amide (Example 3) was compared to the (S)-stereoisomer and racemic mixture thereof and the result is summarized in table 5.

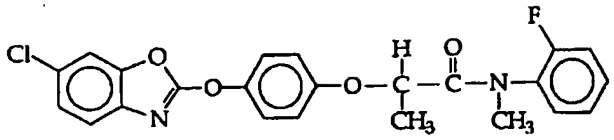
Table 5

Amount of Leaf treatment (g/ha)	(R)-compound		R,S-racemic compound		(S)-compound	
	Rice (4 leaves)	Barnyard grass (4 leaves)	Rice (4 leaves)	Barnyard grass (4 leaves)	Rice (4 leaves)	Barnyard grass (4 leaves)
4000	22.5	100	3.8	100	0.0	100
2000	11.3	100	0.0	100	0.0	100
1000	2.5	100	0.0	100	0.0	100
500	0.0	100	0.0	100	0.0	100
250	0.0	100	0.0	100	0.0	100
125	0.0	100	0.0	100	0.0	100
63	0.0	100	0.0	100	0.0	100
32	0.0	100	0.0	100	0.0	92.5
16	0.0	100	0.0	100	0.0	65.0
8	0.0	98.8	0.0	45.0	0.0	7.5
4	0.0	62.5	0.0	2.5	0.0	0.0
2	0.0	6.3	0.0	0.0	0.0	0.0
1	-	-	-	-	-	-

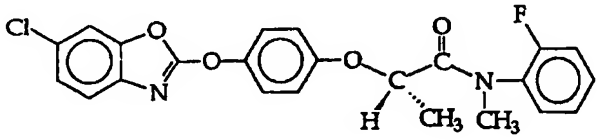
(R)-Compound



R,S-Racemic compound



(S)-Compound



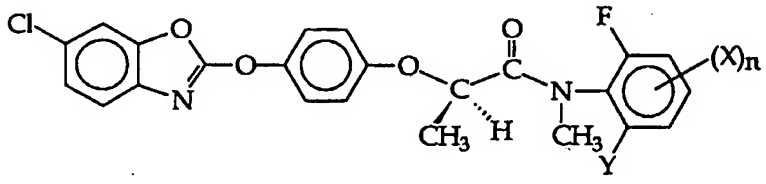
【Industrial Applicability】

As described above, it is noted that optically active (R)-stereoisomers of the present invention exhibit excellent selectivity toward rice and superior herbicidal activity against barnyard grass to racemic mixtures and (S)-stereoisomers thereof. Therefore, the optically active compounds of the present invention may be very effective in rice farming. Further, it is proved that the optically active compounds are very stable for wheat, barley, beans, and corn and useful to control weeds.

[CLAIMS]

What is claimed is:

1. A herbicidal compound, (R)-phenoxypropionic acid-*N*-methyl-*N*-2-fluorophenyl amide of formula (1), having stability toward rice and preventing the generation of barnyard grass:



(1)

wherein X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl;

Y is hydrogen or fluoro; and

n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

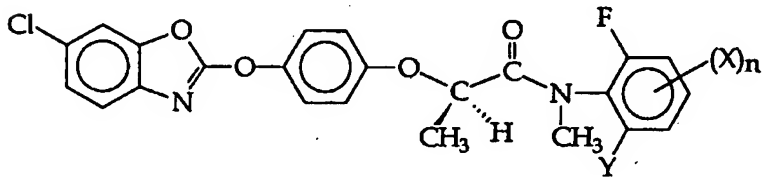
2. The herbicidal compound according to claim 1, wherein said X is H, F, Cl, Br, CN, CH_3, or OCH_3; Y is H or F; and n=1.

3. The herbicidal compound according to claim 1, wherein said X is H; and Y is H.

4. The herbicidal compound according to claim 1, wherein said X is 5-CH_3; and Y is H.

5. The herbicidal compound according to claim 1, wherein said X is 4,5-F_2; and Y is H.

6. A method of controlling barnyard grass produced while growing rice without inflicting any substantial harm to said rice which comprises applying an effective amount of at least one compound of formula (1):



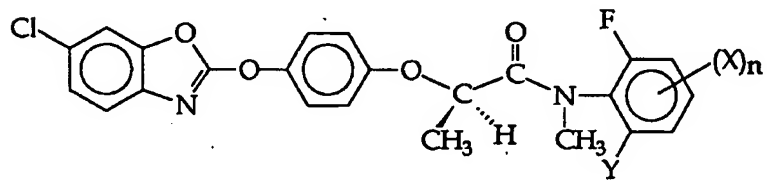
(1)

wherein X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl;

Y is hydrogen or fluoro; and

n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

7. A herbicidal composition comprising at least one compound of formula (1) together with at least one member selected from the group consisting of: an agriculturally acceptable carrier, a supplement agent, a surfactant and at least one other herbicidal compound:



(1)

wherein X is hydrogen, halogen, hydroxy, NH_2, CO_2H, C_1-C_6 alkylamino substituted with 1 or 2 of C_1-C_3 alkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, C_2-C_4 alkoxyalkoxy, C_1-C_4 alkylthonyl, C_1-C_4 alkylsulfonyl, C_2-C_6 alkenyl, C_2-C_6 alkinyl, C_2-C_6 alkenyloxy, C_2-C_6 alkinyloxy, C_1-C_3 alkoxycarbonyl, or C_1-C_3 alkylcarbonyl;

Y is hydrogen or fluoro; and

n is an integer of 0 to 2, wherein X can be a combination of other substituents when n is 2.

INTERNATIONAL SEARCH REPORT

rnational application No.
PCT/KR01/01845

A. CLASSIFICATION OF SUBJECT MATTER

IPC7 A01N 43/38

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7 A01N 43/38, C07C 233/00, C07D 263/52, C09D 5/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/05956((Korea Research Institute of Chemical Technology) 10 February 2000 see the whole document	1-7
A	US 5833742(G. L. Willingham et al.) 10 November 1998 see the whole document	1-7

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevence

"E" earlier application or patent but published on or after the international filing date

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevence; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevence; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 JULY 2002 (18.07.2002)	19 JULY 2002 (19.07.2002)

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR01/01845

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5833742	10-11-98	CN 1181182 A	13-05-98
		CA 2216764 A	11-04-98
		EP 835605 A	15-04-98
		JP 10118659 A	12-05-98
WO 00/05956	10-02-00	CN 1315831 A	03-10-01
		EP 1100332 A	23-05-01
		BR 9912440 A	02-10-01
		AU 5068199 A	21-02-00